REMARKS

Claims 1-21 are pending in the application. Applicants have canceled claims 22-44 as directed to a non-elected invention. Applicants have amended claim 1 to indicate that the functional groups on the membrane are positively charged. This concept is described in the application, e.g., at page 3, lines 31-32. The amendment thus adds no new matter to the application.

The Invention

The invention is based on the discovery that certain membranes, that include side chains or molecular "brushes" having positively charged functional groups, can be used as highly effective filters to capture viruses and virus particles from liquids with minimal removal of proteins. New methods based on this discovery include removing viruses from liquids such as blood or plasma.

Restriction

Applicants confirm the election of Group I, claims 1 to 21, and have canceled claims 22 to 40 without prejudice.

35 U.S.C. § 102

Claims 1 to 5, and 20 have been rejected as being anticipated by Baurmeister et al (6,022,478)(hereinafter '478). Applicants respectfully traverse this rejection for the following reasons.

According to the Office Action, Baurmeister describes, "removing virus using a membrane having the claimed properties (abstract, column 12, last paragraph, column 18, lines 35-61, column 19 last paragraph through column 20, lines 1-38), the virus separation is disclosed in '478 (column 39-55). Applicants disagree.

Applicants have electronically searched the Baurmeister patent, and the word "virus" appears only once in the entire document. The word "virus" appears in the following passage (column 20, lines 38-54):

> Further applications are found in the field of cell selection. In these, use can be made of the feature that when the device in accordance with the invention is used or in conducting the process in accordance with the invention part of the primary stream flows as the secondary stream towards

the membrane wall of the treatment elements and through the walls of the treatment elements. The advantage of this when cell suspensions are used is that cells which are target substances are transported by convection to the membranes and are there brought into direct contact with, for example, ligands immobilized on the exterior of the membrane or the treatment element, which for example identify a certain surface protein of the cells. The devices in accordance with the invention are also most suitable for applications in the field of genetic technology, if such applications call for convective transport for example of genes for instance to viruses or cells immobilized on and/or in the membrane.

As is clear from the context of this passage, Baurmeister describes the use of the membrane for cell selection and genetic technology, and in particular, to convectively transport genes to viruses or cells on or in the membrane. There is no suggestion to use the membrane to remove viruses from a liquid using the Baurmeister membrane. There is no other mention of the use of the membranes with viruses. Therefore, contrary to the assertions in the Office Action, Baurmeister does not anticipate the present method claims, and applicants request that this rejection be withdrawn.

Next, the Office Action has rejected claims 1 to 5, 10, 11, and 18 to 20 as allegedly anticipated by Motomura et al (5,667,684)(hereinafter "Motomura"). Applicants dispute this rejection as well.

According to the Office Action, Motomura discloses removing virus from body fluids with a membrane having the claimed properties. However, there is an important difference in the membrane materials and properties that applicants have now emphasized in the claims. The claimed methods require the use of a membrane engrafted with polymeric side chains having one or more positively charged functional groups. This is exactly the opposite charge of the functional groups that Motomura uses for his membranes.

Motomura describes the use of sulfuric groups and polysulfuric compounds to prepare his membranes (see, e.g., Summary of the Invention at column 2). It is well known that sulfuric groups are negatively charged. Thus, Motomura cannot anticipate applicants' claims, which require functional groups that are positively charged.

The Office Action also notes that as to applicants' claims 10 and 11, Motomura discloses removing virus, e.g., HIV, at a level higher than 95% (column 3, last paragraph, table 4, column 10, line 41). Although this is true, the difference between Motomura's 95% or even 99.5% HIV removal in Table 3, and applicants' claimed "at least 99.999%" or "at least 99.99999%" virus removal, is enormous. For example, 99.5% virus removal means that

of 100,000 viral particles, 99,500 are removed and 500 remain. However, 99.999% viral removal means that of 100,000 viral particles, only 1 viral particle remains. Thus, the claimed methods are at least 500 times more effective than Motomura's method that removes at most 99.5% of viral particles. Applicants' claim 11 requires 99.99999% virus removal, which is 50,000 times more effective than Motomura's method. Thus, claims 10 and 11 are clearly not anticipated by Motomura.

Applicants' claims 18 and 19 cover eluting the virus particles from the membrane after the virus particles are separated from the liquid. The Office Action seems to mischaracterize Motomura, because this reference does not describe eluting the virus and does not describe the use of a sodium chloride solution. Instead, Motomura describes the use of sodium hydroxide to neutralize the membrane, and then rinsing with water and treating the membrane with dilute hydrochloric acid and rinsing with water. None of these treatments have anything to do with eluting virus from the membrane, but are used to prepare the membranes. Thus, in addition to the fact that claims 18 and 19 depend from claim 1 and are thus not anticipated, they are also not anticipated for this additional reason.

35 U.S.C. § 103

Claims 6 to 9, 12 to 15, 17, and 21 have been rejected as allegedly unpatentable over Motomura. Applicants traverse this rejection for the reasons noted above and for the following reasons.

The Office Action concedes that Motomura "fails to disclose the limitations of the [dependent] claims" (at pages 3-4), but alleges that these claims are nonetheless obvious. However, all of these claims are dependent claims, and thus are not obvious for the same reasons that claim 1 is not obvious, i.e., claim 1 recites positively charged functional groups, and Motomura describes negatively charged sulfuric functional groups. There is no suggestion in Motomura to use anything other than negatively charged sulfonic acid functional groups.

However, some of the dependent claims are also not obvious for additional reasons. For some dependent claims, Motomura does not provide sufficient information to determine whether there is a specific difference between applicants' claims and Motomura's methods. For example, claims 13 and 14 require that certain levels of proteins be removed from a sample. Applicants' methods are highly effective in that they remove very little protein, e.g.,

less than 10% or less than 2% (claims 13 and 14, respectively). Motomura fails to disclose the precise amounts of protein that his method removes, but is not specific, so a direct comparison cannot be made.

For other claims, applicants can more easily distinguish their claims from Motomura's disclosure. For example, with respect to claim 15, Motomura is silent as to the effect his methods have on plasma clotting times. Thus, there is simply no support for the alleged obviousness of claim 15, which recites that when the sample is a plasma sample, that the method results in less than a five-fold increase in the plasma's clotting time. Contrary to the assertion in the Office Action, this specific feature cannot be determined from the degree of virus removal.

With respect to claims 18 to 21, applicants submit that Motomura does not describe or suggest eluting the virus from the membrane and preparing a concentrated or purified solution of the virus. In fact, since Motomura describes only HIV, there is little reason for him to create a concentrated and purified solution of virus. Thus, applicants' claims 18 to 21, which relate to preparing a purified virus concentrate, cannot be rendered obvious by Motomura.

Based on the patentability of claim 1 over Motomura, and the additional reasons discussed above, dependent claims 6 to 9, 12 to 17, and 21 are also patentable over Motomura. Applicants note that claim 16 is not recited in the list of claims rejected under Section 103 on page 3 of the Office Action, but assume that the Examiner intended to include this claim in the rejection.

CONCLUSION

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. No excess claims fees and no Extension of Time fees are required. However, please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 00786-429001.

Respectfully submitted,

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Version with Markings to Show Changes Made

In the claims:

Claims 22 to 40 have been canceled without prejudice.

Claim 1 has been amended as follows:

-- 1. (Amended) A method for removing a virus from a liquid sample, the method comprising:

obtaining a membrane engrafted with polymeric side chains having one or more positively charged functional groups that interact with viruses, wherein the membrane has a nominal pore size between 20 nm and 1000 nm; and

passing the sample through the membrane to remove viruses from the sample.--